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inserted into a test apparatus such as shown and described in detail in U.S. Pat. 4,599,219 ("the '219 patent") for the determination of clotting time of an aliquot blood sample inserted into each test cell 11 as described in detail in said patent." In particular, the Examiner's attention is directed to columns 3, 13-17, and 24-25, and Figures 16, 17 and 24A-D of the '219 patent for a description of the apparatus used in the method of the present invention. For example, the '219 patent states that the plunger sensor cartridge includes a plunger assembly which is lifted by an actuator mechanism (column 3 at lines 51-55). The actuator mechanism includes a lift wire 372 (column 16, lines 16-53) that acts to lift all of the plungers at the same time and at the same rate (column 17, lines 20-32 and column 24, lines 9-30).

In addition, claims 17-21 and 26-29 have been amended to correct the claim number from which they depend as a result of the Examiner's renumbering of the claims in the previous office action. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

Rejections under Obviousness-Type Double Patenting

Claims 4-6, 8, 10-12, 14, 16, 18-22, 24 and 26-28 are rejected under the judicially created doctrine of double patenting as being unpatentable over claims 28-40 of U.S. Patent No. 5,972,712, respectively. The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because both teach method of evaluating the clotting characteristics of blood. A Terminal Disclaimer with respect to U.S. Patent No. 5,972,712 will be filed when patentable subject matter has been determined.

Rejection under 35 U.S.C. § 103(a)

The rejection of claims 4-6, 8, 10-12, 14, 16, 18-22, 24 and 26-28 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,314,826 to Baugh ("the '826 patent") in view of U.S. Patent No. 4,329,302 to Hanahan et al. ("the '302 patent") was maintained. The Office Action states that Baugh teaches a method for the evaluation of clotting characteristics of platelets but is silent to the claimed 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine (AGEPC). The Office Action then states that Hanahan teaches that AGEPC is a potent platelet activator, and concludes it would have been within the skill of the art to modify Baugh in view of Hanahan et al. and use AGEPC to gain the advantage of high platelet activation. This rejection is respectfully traversed.

Independent claims 4, 8 and 25 have been amended herein to further distinguish the

claims over the cited art by clarifying which factor is varied in order to evaluate the contribution of platelet activation to the activated clotting time test. The variable factor in the present invention is clearly different than that in the Baugh method, as discussed below in detail, and therefore the claimed methods are not obvious in light of the cited references.

To clarify this fundamental difference, claim 4 as amended herein is directed to a method for determining platelet functionality of a blood sample using a plunger sensor apparatus comprising two or more test cells and a plunger assembly within each test cell, wherein the method includes the step of performing a clotting test on the aliquot samples by alternately lifting the plunger assembly in each cell and allowing the plunger assembly to descend through the test mixture, wherein all of said plunger assemblies are lifted in unison. Claims 8 and 25 each contain similar language to indicate that all of the plungers are reciprocated at the same rate. It is believed that such claim limitations clearly distinguish the claimed invention over the cited art for the reasons presented below.

Baugh teaches a method of evaluating platelet functionality which also uses a plunger sensor apparatus; however, the Baugh method comprises two separate phases. The first phase of the test, termed the "platelet activation phase," activates the platelets by mechanical means, as opposed to chemical means using a platelet activating factor as taught and claimed in the present invention. The platelet activation phase of the Baugh method requires a controlled predetermined activation phase in which a predetermined degree of accountable platelet activation can be obtained and taken into account in determining the activated clotting time (column 5, lines 58-63). Following the platelet activation phase, the ACT test continues though a clotting test phase which follows the usual procedure of the particular ACT test being performed.

More specifically, and with reference to Figures 8A and 8B of the '826 patent, the Baugh method comprises two separate ACT tests 130 and 134, which can be run simultaneously or sequentially (column 11, lines 16- column 12, line 14). The first ACT test (130) has a platelet activation phase (132) with a predetermined **low** intensity of agitation to achieve a relatively higher rate of contribution from platelet activation to the ACT. The second ACT test (134) has a platelet activation phase (136) with a predetermined **higher** intensity of agitation selected to achieve a relatively lower rate of contribution from platelet activation to the ACT. That is, the degree of agitation during the first phase of the Baugh method differs between the two tests (130) and (134). In order to achieve these differing intensities of agitation, the plungers in the respective test cells must be lifted and lowered at

different rates (column 11, lines 56-60). This is accomplished either by utilizing one ACT apparatus comprising an assembly apparatus that is designed to reciprocate the plungers independently, or by using two separate ACT apparatuses.

In summary, the Baugh method teaches a two-phase platelet functionality test comprising a separate platelet activation phase. This separate phase of the test establishes the rate of contribution of platelet activation to the ACT test by mechanically activating the platelets. Thus, the variable in the Baugh method is the rate of agitation in each test (with all other factors held constant). In order to achieve this, the Baugh method requires a means of providing different rates of agitation to various test cells.

In contrast, the method of the present invention is directed to a method of determining platelet functionality or clotting characteristics of a blood sample wherein the contribution of platelet activation to the ACT test is established by chemically activating the platelets. That is, platelets are activated by adding varying amounts of a platelet activating factor to each test cell. Thus, the variable in the present invention is the amount of platelet activating factor that is added to each test cell, with all other factors, including the rate of plunger reciprocation, held constant. This required feature of the claimed method further supports the claim amendments presented herein. That is, if the amount of platelet activating factor in each test cell is varied, then clearly all other factors in the method of this invention (including the rate of reciprocation of the plungers) must be held constant in order to obtain a titration curve as described on page 8 of the specification.

Further, it is asserted if the method of Baugh was modified by adding the platelet activating factor as taught by Hanahan, one would not be able to determine the contribution of platelet activation to the ACT test, since the method would then contain two variables that affect platelet activation, namely, the different rates of agitation and the different amounts of the platelet activating factor. Accordingly, such a modification would render the Baugh et al. invention inoperative. "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." *In re Gordon*, 733 R.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Accordingly, it is asserted that it would not have been obvious to modify the teaching of Baugh with the teaching of Hanahan as stated in the Office Action to arrive at the method of the present invention. Further, there is no motivation to modify the method of Baugh by adding a platelet activating factor, since the Baugh method already includes a means for

activating platelets. Hence, claims 4-6, 8, 10-12, 14, 16, 18-22, 24 and 26-28 are allowable over the combination of Baugh with and Hanahan. Withdrawal of the Section 103(a) rejection is respectfully requested.

CONCLUSIONS

It is believed that all the claims now pending in this patent application, as amended and described above, are now allowable. Therefore, it is respectfully requested that the Examiner reconsider his rejections and to grant an early allowance. If any questions or issues remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number listed below.

It is believed that no fees are required in filing this Amendment and Remarks. However, should any fee be required, please charge Deposit Account No. 50-1123.

Respectfully submitted,

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Dated

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MARKED UP VERSION SHOWING CHANGES MADE TO CLAIMS

Please amend claims 4, 8, 17-20, and 24-28 as follows.

4. (Three times amended) A method for determining platelet functionality of a blood sample using a plunger sensor apparatus comprising [at least one test cell] two or more test cells and a plunger assembly within [said] each test cell, the method comprising:

(a) dispensing an aliquot of said sample into each of said test [cell] cells;

(b) adding a selected amount of a platelet activating reagent to all but one of said aliquot [sample] samples to form a reaction mixture;

(c) adding a sufficient amount of a clotting reagent to each of said reaction [mixture] mixtures to promote clotting of said aliquot [sample] samples;

(d) performing a clotting test on said aliquot [sample] samples by alternately lifting the plunger assembly in each cell and allowing the plunger assembly to descend through the test mixture, wherein all of said plunger assemblies are lifted in unison; and

(e) determining said platelet functionality of said sample [based on] by comparing the clotting times [for] of said aliquot [sample] samples, wherein said clotting time of each aliquot sample is determined by measuring a change in viscosity of each of said aliquot [sample] samples.

8. (Three times amended) A method for determining clotting characteristics of a blood sample using a plunger sensor apparatus comprising [at least one test cell] two or more test cells and a plunger assembly within [said] each test cell, said method comprising:

(a) dispensing an aliquot of said sample into each of said test cell;

(b) adding a selected amount of a clotting affecting reagent to all but one of said aliquot [sample] samples to form a reaction mixture;

(c) adding a sufficient amount of a clotting reagent to each of said reaction [mixture] mixtures to promote clotting of said aliquot [sample] samples;

(d) performing a clotting test on said aliquot [sample] samples by alternately lifting the plunger assembly in each cell and allowing the plunger assembly to descend

through the test mixture, wherein all of said plunger assemblies are lifted in unison; and

(e) determining the clotting characteristics of said sample [based on] by comparing the clotting times [for] of said aliquot [sample] samples.

17. (Amended) The method of claim [18] 16, wherein said platelet activating reagent is 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine.

18. (Twice amended) The method of claim [26] 24, wherein the amount of said platelet activating agent in each said aliquot sample is between about 0 and about 2.76 micrograms.

19. (Twice amended) The method of claim [26] 24, wherein the concentration of said platelet activating reagent in each said aliquot sample is between about 0 and about 150 nM.

20. (Twice Amended) The method of claim [26] 24, wherein at least one of said aliquot samples contains no platelet activating reagent, and wherein each remaining aliquot sample comprises different amounts of said platelet activating reagent.

24. (Twice Amended) A method for performing an activated clotting time test on a sample of blood using a plunger assembly apparatus comprising a multicell test cartridge, said cartridge comprising at least a first, a second and a third test cell and a plunger assembly within each of said test cells, each of said cells comprising a sufficient amount of a contact activator to achieve clotting, wherein said first cell further comprises a first amount of a platelet activating reagent and wherein said second cell comprises a second amount of said platelet activating reagent, said first and second amounts being different, said method comprising:

(a) dividing said sample into first, second and third partial samples;

(b) dispensing the first partial sample into the first test cell to form a first test mixture;

(c) performing a first activated clotting time test on the first test mixture by reciprocating said plunger assembly within said first cell to obtain a first clotting time;

(d) repeating the aforementioned steps of dispensing and performing an activated clotting time test on each of said second and third partial samples by reciprocating the plungers in said second and third cells at the same rate of reciprocation as in said first cell to obtain a second and third clotting time; and

(e) comparing the clotting time of said first, second, and third partial samples to

determine the activated clotting time of the sample of blood based on the clotting time times of said first, second and third partial samples.

25. (Twice Amended) The method of claim [26] 24, wherein said platelet activating reagent is selected from the group consisting of 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine, collagen, epinephrine, and ristocetin.

26. (Amended) The method of claim [26] 24, wherein said platelet activating reagent is 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine.

27. (Amended) The method of claim [26] 24, wherein said clotting reagent is kaolin.

28. (Amended) The method of claim [26] 24, wherein said clotting times are determined by measuring a change in viscosity of each of said aliquot samples.